False-positive blood cultures in a patient with acute myeloid leukemia

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A 56-year-old female was admitted because of a 3-week history of malaise and fever. On admission, the patient was critically ill and her temperature was 39°C. After blood cultures were drawn, empirical antibiotic therapy was started (piperacillin and amikacin). Four blood-culture sets (BACTEC^{PLUS}/F, aerobic and anaerobic bottle) were incubated, and two bottles (of different sets) were flagged positive by the BACTEC 9240 system (Becton Dickinson Diagnostic Instrument Systems, Meylan, France). Times to detection were 19.1 and 4.3 h for the aerobic and the anaerobic bottles, respectively. Gram-stained smears of the blood-culture medium revealed no organisms, and aerobic as well as anaerobic subcultures remained sterile. A false-positive signal was suspected, and the curves of growth index values of the bottles were visualized. The shapes of these curves were indistinguishable from those observed during bacterial growth. On acridine orange staining of the blood-culture medium, no bacteria were observed but an exceptionally high number of leukocytes was seen. The white blood cell count of the patient was high (446×10^9/L) and consisted of almost 100% blasts. Examination of bone marrow led to the diagnosis of acute myeloid leukemia (ML).

Blood cultures are routinely used whenever the presence of clinically significant bacteremia is suspected [1]. Several automated blood-culture systems have been developed over the past three decades [2,3]. The introduction of automated blood-culture systems has enabled an optimal microbiological yield, associated with a decrease in detection time and a reduction of the laboratory workload. In our hospital, the BACTEC 9240 system is used. A pH-sensitive sensor is embedded in an inert matrix at the bottom of the BACTEC^{PLUS}/F bottle. Growth of organisms produces carbon dioxide in the broth, which in turn causes a pH change that is detected by a fluorescent dye in the sensor. If the course of the pH changes meets the specific criteria outlined in the BACTEC software, the blood-culture bottle is flagged as positive by the device. Some of the positive blood cultures qualify as false positive, and should be distinguished from contaminated blood cultures. 'False positive' (FP) refers to blood-culture bottles that are flagged by the automated blood-culture system but that show no microorganisms in the Gram-stained smear and from which appropriate subculture fails to demonstrate microorganisms. FP blood cultures require technologist time and may affect patient care, as they can lead to the unnecessary administration of antimicrobial agents. In recent studies on automated blood-culture systems, FP rates (expressed as percentage of the total number of blood cultures) ranged from 0.7% to 6.2% [4,5]. We recently performed two audits on the volume of blood submitted for culture, during the periods 1996 and 1997, on more than 8500 blood-culture bottles for each year [6]. During these audits, we found FP rates of 1.8% and 0.8% for the years 1996 and 1997, respectively. The decrease in the FP rate in the period 1997 coincided with the implementation of an updated version of the BACTEC software (V3.61). During these audits, we further observed a significant relationship between overfilling of the BACTEC^{PLUS}/F bottles (i.e. volumes $\geq$10 mL) and the FP rate [6], with 98 of 159 (61%) FP bottles being overfilled. This is in line with the findings of Alfa et al, who found the majority (16/17, 95%) of their FP BacT/Alert bottles to be overfilled [7]. The authors suggested that the CO_2 generation from leukocyte respiration in the large blood volumes might be sufficient to cause a positive signal by the automated system but did not further investigate this phenomenon.

The present case illustrates an FP event probably caused by non-microbial CO_2 generation in a patient with myeloid leukemia. The blood-culture bottles of the present patient were not overfilled. The total white blood cell count of 446×10^9/L, however, accounted for nearly half of the total blood cell mass. To our knowledge, in the English language literature there is only one communication on the association of FP blood cultures and hyperleukocytosis [8]. Martinez et al described two FP blood cultures in both the BACTEC NR730 and BacT/Alert systems. In line with the present case, the FP blood cultures observed by these authors were obtained from a patient with acute myeloid leukemia presenting with an elevated number of circulating leukocytes (150×10^9/L, 95% blasts). Both cases illustrate the association of FP blood-culture bottles with high leukocyte counts and point to cell respiration or, alternatively, lysis of the cells as the factor responsible for the pH change. Further study of this phenomenon is needed to clarify the exact mechanism and allow adequate refinements of the detection system.

Blood cultures are part of the microbiological work-up of febrile patients in the hematologic unit. The present case illustrates the association of a high circulating leukocyte count with an FP reading of blood-culture bottles. This should be kept in mind

when interpreting positive signals generated by automated blood-culture systems.

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Rhabdomyolysis in acute Q fever

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Acute Q fever is a non-specific febrile illness caused by *Coxiella burnetii*. The most common clinical presentations of acute *C. burnetii* infection are atypical pneumonia and hepatitis [1]. Other complications of acute Q fever include hemolytic anemia, myocarditis, pericarditis, pancreatitis, thyroiditis, mesenteric panniculitis, mediastinal lymphadenopathy, orchitis, erythema nodosum and optic neuritis [2]. However, rhabdomyolysis is an apparently uncommon complication of *C. burnetii* infection, and this association has rarely been reported [3–8]. Here we report another case of severe rhabdomyolysis secondary to acute Q fever.

A 75-year-old man was admitted to our hospital because of a 24–36 h history of fever, chills, malaise, myalgias and severe muscular weakness. He had had frequent contact with livestock. On admission, temperature was 38.8°C and blood pressure 130/80 mmHg. Physical examination was unremarkable. White blood cell count was 10.7×10^9/L (76% neutrophils, 19% band forms, 1% lymphocytes, and 4% monocytes), hemoglobin level was 15 g/dL and platelet count was 133×10^9/L. Laboratory tests revealed serum creatinine 3.4 mg/dL, urea 193 mg/dL, creatine kinase 21835 U/L (MB fraction 120 U/L), lactate dehydrogenase 679 U/L, aspartate aminotransferase 436 U/L, alanine aminotransferase 165 U/L, and a normal bilirubin value. Antinuclear antibodies, rheumatoid factor, and antineutrophil cytoplasmic antibodies were negative. Chest radiographs and thoracic and abdominal computed tomography were normal. Cultures of blood and urine were sterile. Antibodies against *C. burnetii* were not determined during the hospitalization period. Therapy with cloxacillin and ciprofloxacin was empirically started and was followed by a clear improvement in the patient's condition. He was discharged after 11 days of treatment. One month later, the patient was asymptomatic and the abnormal laboratory tests had became normal. Serologic tests for *Leptospira*, *Brucella*, syphilis and *Borrelia burgdorferi* were negative. The titer of IgG antibodies to phase II antigen of *C. burnetii* determined by the indirect immunofluorescence test (bioMerieux, Marcy l'Etoile, France) was 1/2048, and IgM antibodies were positive. Four months after the onset of symptoms the titer of antibodies had fallen to 1/256.

Although, unfortunately, seroconversion could not be confirmed in this patient because of the lack of an earlier serum sample, the positivity of IgM and the very high titer of IgG antibodies 45 days after the onset of symptoms strongly suggest acute Q fever. In addition, the decrease in the titer of antibodies observed several months later suggests that the first determination corresponded to the peak titer of antibodies. Our patient presented with transient acute renal failure due to rhabdomyolysis, like one of the seven cases previously reported [4]. Myoglobinuric renal failure, which complicates up to 30% of cases of rhabdomyolysis, is the result of the toxic effects of myoglobin on tubule epithelial cells [9]. However, pathogenetic mechanisms of rhabdomyolysis in acute Q fever are unclear. Nevertheless, some authors have suggested that rhabdomyolysis in these patients might be a consequence of release of an endotoxin or exotoxin [3].

It is interesting that all patients reported with muscle injury associated with acute Q fever, like our patient, were from Spain, considering that there is no evidence that the Spanish strains of *C. burnetii* have a particular muscular tropism. However, the manifestations of this infection may differ from country to